UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/037,791	01/03/2002	Stanley M. Crain	96700/727	7711

7590 02/19/2003

Craig J. Arnold
Amster, Rothstein & Ebenstein
90 Park Avenue
New York, NY 10016

EXAMINER	
REAMER, JAMES H	
ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 02/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/037,791	Applicant(s) CRAIN ET AL.	
	Examiner James H. Reamer	Art Unit 1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 30-48 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☒ Claim(s) 30-48 is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 30-33 and 40-44 are rejected under 35 U.S.C. 102(b) as being anticipated by Levine et al (46). Levine teaches potentiation of the pentazocine analgesia by low dosage. See page 1574, second column under Methods. The ratio of pentazocine to naloxone taught by Levine et al is 150:1 and these compounds are the same compounds as the compounds of the claimed invention agonist ant antagonist, respectively.

Claims 36 and 46 are rejected under 35 U.S.C. 102(b) as being anticipated by Levine et al (46). Levine et al teach administration of morphine combined with low-dose naloxone to human patients via IV. This drug composition, the amounts, the subject, the manipulative steps appear to be the same as those encompassed by the methods of the instantly claimed invention.

Claims 30-32 and 36 are rejected under 35 U.S.C. 102(b) as being anticipated by Lewenstein (3,493,657). Lewenstein discloses the use of a therapeutic composition comprising morphine and naloxone to provide a strong analgesic as well as antagonistic effect without the occurrence of undesired or dangerous side effects. See example 8, column 3, line 44 through column 4, line 3. The reference teaches the dosage for

humans ranging from 3 to 30 mg of morphine to o.001 to 3 mg of naloxone (ie 300-10 fold less naloxone as compared to the amount of morphine).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 33, 40-44 and 46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lewenstein. Furthermore, Lewenstein discloses the modes of administration, iv, im, sc, for the compositions of naloxone and strong analgesic. See column 2, lines 70-73; column 3, lines 9. It would be obvious to one of ordinary skill in the art to utilize the composition taught by Lewenstein to administer via well known established method to treat patients suffering pain since the references exemplify such parenteral routes to administer analgesic compositions, wherein the analgesics were well known to treat pain with a reasonable expectation of relieving pain with morphine compositions, without the unwanted side effects of morphine as taught by the reference. The use of the composition in the method taught by the reference wherein the ration of morphine to naloxone is at least 100:1 would have been obvious since the reference

teaches an overlapping useful range of 10 to 300 fold less naloxone as being effective, in the absence of evidence of criticality or unexpected results.

Claim Rejections - 35 USC § 102

Claims 30-40 are rejected under 35 U.S.C. 102(b) as being anticipated by Pachter et al (3,879,555). Pachter et al disclose methods of treating drug addictions with orally effective analgesic compositions comprising opioid agonists in combination with opioid antagonist. See column 4, lines 11-55, and column 6, and lines 34, 39-44 and column 11, example 7.

Claim Rejections - 35 USC § 103

Claims 41-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pachter et al, cited above. Pachter et al does not particularly exemplify a method for treating pain, it teaches a method for producing analgesia and discloses that the utility of the analgesics in treatment of various conditions. See column 2, lines 13-34 and column 7, lines 58-67. It would have been obvious to one skilled in the art to apply the method of Pachter et al to treat pain since it is well recognized in the art to relieve pain with opioid analgesics. Since the reference teaches that the methods of using the analgesics in combination with antagonist naltrexone prevent the well known adverse side effects, one skilled in the art would have been motivated to apply Pachter et al's method in treating pain, with a reasonable expectation of obtaining pain relief without the addiction potential as taught by Pachter et al.

Claim Rejections - 35 USC § 102

Claims 30-33, 36 and 38-40 are rejected under 35 U.S.C. 102(b) as being anticipated by Pachter et al (3,773,955). Pachter et al disclose a method of treating drug addicts with a composition comprising opioid agonists in combination with naloxone as a potent, orally effective, but parenterally inactive analgesic medicine useful for treatment of various conditions without addiction and to reduce drug abuse potential. The references teach that the strong analgesics opioid agonists are known to provide relief of severe pain but usually produce euphoric effect on parenteral administration and lead to addiction and abuse. Pachter et al invented a composition what contains a parenterally effective but orally ineffective dose of opioid antagonist such as naloxone and an orally analgesic dose of an orally effective strong analgesic such that that the composition can be administer orally and not interfer with the analgesic effect of the opioid agonist. These compositions may be administered parenterally without causing euphoria. The effective dosage ratios taught by the reference overlap the claimed ranges. The oral administration of the composition taught by Pachter et al must inherently produce the claimed benefits sought by the instant application since the two methods are the same.

Claim Rejections - 35 USC § 103

Claims 33, 41-44 and 46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pachter et al, cited above. Pachter et al further discloses that the strong analgesics have been employed in the relief of more severe pain but that they

usually produce euphoric effect on parenteral administration. It would be obvious to one skilled in the art to use the composition taught by Pachter et al to relieve pain since the composition does not produce the adverse euphoric side effects. Furthermore, the use of the analgesic composition of greater than 100 fold more than antagonist in such a method would have been obvious in view of the prior art's teachings for about 80 parts pentazocine and up to 150 codeine with one part naloxone, in the absence of criticality to the claimed range.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 32 and 34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The metes and bounds of "similarly acting opioid alkaloids and opioid peptides". It is unclear if the "similarly acting" compares to the recited compound species or the activities recited in the independent claims. Deletion of the phrase is suggested.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re*

Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 30 to 48 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim1-32 of U.S. Patent No. Re 36,547, 1 to 31 of U.S Patent No. 6,362,194,, claims 1-7 of U.S. Patent No. 6,096,756. claims 1-18 of U.S. Patent No. 5,762,125 and claims 1-10 of U.S. Patent 5,472,943. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the patents are drawn to the same or similar method of using the opioid agonist/ antagonist compositions of the instantly claimed invention wherein the recited are overlapping or appear to be inherent benefits to the instantly claimed methods.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James H. Reamer whose telephone number is (703) 308-4461. The examiner can normally be reached on 5:30 AM to 2:00 PM Monday-Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel can be reached on (703) 308-4725. The fax phone numbers for the organization where this application or proceeding is assigned are (703)

872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

James H. Reamer
Primary Examiner
Art Unit 1614

JHR
February 14, 2003